



Patent 09/772,644
Attorney's Docket No. 0033072-007

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)	
Lawrence S. Barak et al.)	Group Art Unit: 1632
Application No.: 09/772,644)	Examiner: Anne-Marie Falk, Ph.D.
Filed: January 30, 2001)	Confirmation No.: 1059
For: Methods of Assaying Receptor Activity)	
and Constructs Useful in Such Methods)	
)	
)	

TECH CENTER 1600/2900

APR 07 2003

RECEIVED

DECLARATION BY INVENTOR UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Mark G. Caron, Ph.D. hereby state as follows:

1. I am an inventor named in the above-identified application ("the patent application"). I am a B. Duke Professor of Cell Biology at Duke University where I have been involved generally in the area of research concerning G Protein Coupled Receptors (GPCRs) for about 30 years. I also teach Cellular Signaling (CBI417) to graduate students and was teaching graduate students at the time the application was filed. My CV is attached as Exhibit 1 which includes a list of my publications.
2. As explained below, a typical graduate student active in research concerning GPCRs reading the application would know how to make and use a variety of biologically active labeled arrestin proteins with little or no experimentation.
3. At the time the patent application was filed, a variety of arrestins had been identified, characterized, and cloned. Numerous papers were written describing a variety of arrestin proteins and their interaction with GPCRs:

Retinal arrestin was determined in 1992 and disclosed in
Shinohara et al. "A family of retinal S-antigens (arrestins) and
their genes: Comparative analysis of human, mouse, rat,
bovine and *Drosophila*." Comp. Biochem. Physiol. B 103: 505-
509. Copy attached as Exhibit 2.

Splice variants of human β -arrestin-1 and arrestin were identified in 1993. Perruti et al. "Molecular analysis of human β -arrestin-1: Cloning, tissue distribution, and regulation of expression. Identification of two isoforms generated by alternative splicing. " J. Biol. Chem. 268:9753-9761. Copy attached as Exhibit 3.

In 1993, Murakami et al. disclosed a retinal cone-specific homolog of arrestin. "A new retinal arrestin mapping to the X chromosome" FEBS Lett 334:203-209. Copy attached as Exhibit 4.

"Arrestin interactions with G protein-coupled receptors" Gurevich et al., J. Biol. Chem. (1994) 270:2 720-731 describes direct binding studies of wild type and mutant arrestins with rhodopsin, β_2 -adrenergic, and m2 Muscarinic cholinergic receptors. Copy attached as Exhibit 5.

"Structure and functions of arrestins", Protein Science (1994), 3:1355-1361 discloses sequence alignment of bovine arrestin with its homologs. Copy attached as Exhibit 6.

A 1996 paper entitled "G-protein-coupled receptor regulation: role of G-protein-coupled receptor kinase and arrestins" Can. J. Physiol. Pharmacol. 74: 1095-1110 (1996) discloses visual arrestin, β -arrestin 1, β -arrestin 2, and cone arrestin. The article further discloses how these arrestins interact with GPCRs in GPCR arrestin binding. Copy attached as Exhibit 7.

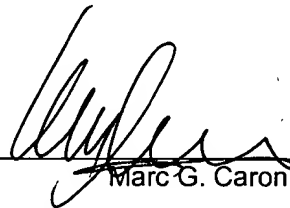
4. The patent application teaches the use of arrestins defined as "all types of arrestin, including but not limited to visual arrestin (sometimes referred to as Arrestin 1), β -arrestin 1 (sometimes referred to as Arrestin 2), and β -arrestin 2 (sometimes referred to as Arrestin 3)."

See page 12, lines 21-24. Specific examples of biologically active labeled β -arrestin proteins are included in the patent application. A typical graduate student active in research concerning GPCRs reading the patent application in view of the literature described above, would know how to make and use a variety of biologically active labeled arrestin proteins with little or no experimentation.

I hereby declare that all statements made herein are of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date:

2/24/2003



Marc G. Caron

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on 3-26-03
Date

Donnie S. Dietrich
(Typed or printed name of person signing the certificate)

Donnie S. Dietrich
(Signature of person signing the certificate)

March 26, 2003
(Date of Signature)